REMARKS

Claims 72 and 74 - 91 are pending in the current application. Claims 1-71 and 73 were previously cancelled. Claim 72 has been amended for purposes of clarity and to provide a clear antecedent for the recitation of the emulsion.

Rejections under 35 USC §§101 & 112

All prior rejections under 35 USC §§101 and 112 have now been withdrawn by the Examiner.

Rejections under 35 USC §102& 103

All prior rejections under 35 USC §102 have now been withdrawn by the Examiner. Additionally, the prior rejections under 35 USC §103 based on Foldvari et al. in view of Mackles, Foldvari et al. in view of Bott, and Foldvari in view of Kosal have all been withdrawn. However, the Examiner has again instituted new grounds of rejection under §103 in this third non-final action.

Rejection of Claims 72 and 74-91 under 35 USC §103 as unpatentable over Kosal in view of Bott et al. and Woodward et al.

In the most recent Office Action, the Examiner has now elevated Kosal to primary status, dropped Foldvari, and has combined Kosal with Bott. Applicants submit that the Examiner has failed to establish a prima facie case for obviousness because she has failed to establish a proper basis for combining the teachings of the references.

Kosal is directed to silicone pressure sensitive adhesive compositions which comprise a disperse silicone phase in a continuous aqueous phase, i.e., and oil-in-water emulsion. Kosal lists a number of different potential uses for the adhesive including

> "paper coatings, such as adhesive labels and sealing strips, in adhesive modifiers such as release modifying additives for organic pressure sensitive adhesives, in personal care applications to give greater durability, protective qualities, water resistance and barrier properties, for example in eye cosmetics such as mascara and in sunscreen formulations as described in U.S. Pat. No. 5,451,610, and in medical applications such as transdermal drug delivery patches, described for example in U.S. Pat. No. 5,162,410, or to hold an active material such as a fungicide to the skin surface. The avoidance of hydrocarbon based solvents is generally desirable in medical and personal care applications, and also

in paper coating applications where evaporation of organic solvent can be a fire hazard." [col. 5, lines 17-30]

In the Office Action, the Examiner conceded that Kosal does not teach that the hydrophilic phase of the adhesive composition contains a protein active agent (Action, page 4). Indeed, Kosal is directed to a silicone-based pressure sensitive adhesive. However, the Examiner asserted that one skilled in the art would have been motivated "to combine the teachings of Kosal and Bott et al. and prepare [sic, an] O/W emulsion comprising the hydrophobic phase with silicone PSA taught by Kosal for transdermal delivery of protein active agents." The Examiner found "motivation" in Kosal's teaching of providing "controlled tack free of hydrocarbon based solvents" and the enablement of holding the active agent to the skin surface (Action, p. 5).

Initially, applicants disagree with the Examiner's interpretation of Kosal with respect to any teaching concerning controlled release of an active agent. Specifically, applicants' claims are directed to a controlled-release composition and method of delivery. As described in the specification, the term "controlled-release" is defined to mean that the active agent is released in a controlled manner over time ("sustained release") from the composition (see, e.g., Examples 1-8). Kosal is silent concerning any controlled release properties of his pressure sensitive adhesive composition. That is to be expected, as the Kosal specification is directed primarily to the adhesive composition and its properties, and not to any specific active agents which may be released over time.

Given this, Kosal's mention at col. 5, line 18, that the described pressure sensitive adhesives may find use "as release modifying additives for organic pressure sensitive adhesives" must be understood in proper context to be directed to the ability of the adhesive compositions, when blended with other "organic"-based adhesives, to modify the *adhesive release characteristics* of those adhesives. That is, the adhesive characteristics or properties of organic pressure sensitive adhesives may be "modified" by the addition of the Kosal adhesives. This is completely different from the meaning of "controlled-release" in applicants' specification and claims, and has nothing whatsoever to do with controlling the release of an active agent contained within the adhesive.

The prior art Bott et al. composition is very different from the presently-claimed composition. In fact, they are the opposite of each other. Bott et al., commonly assigned and

having common inventors, is directed to a topical preparation comprising a continuous silicone phase and a discontinuous phase comprising a hydrophilic carrier and at least one active agent for release from the preparation (see, e.g., paras. [0006], [0033], and [0034]). Unlike Kosal, Bott teaches the use of a *continuous* silicone phase ("silicone matrix") and a *discontinuous* aqueous phase which would be understood by persons skilled in the art to be a water-in-oil composition in which the hydrophilic carrier containing the active agent is dispersed throughout a silicone matrix (see, e.g., para. [0008]).

Thus, in Bott's preparation, a hydrophilic phase containing the active agent and hydrophilic carrier is emulsified with a silicone phase to produce discrete droplets of the aqueous phase dispersed into a continuous silicone phase. The emulsion is then cast and dried, resulting in droplets of the aqueous phase containing the active agent entrapped within the continuous silicone phase. Bott suggests that several mechanisms could be involved in controlling the release of the active agent from the preparation including the addition of hydrophilic agents to the silicone phase or choosing a silicone having a low cross-link density. See, e.g., paras. [0035] and [0058].

The claimed controlled-release composition, on the other hand, is formed by emulsifying silicone and hydrophilic phases, but producing a *continuous* hydrophilic phase containing the active agent with a *discontinuous* silicone phase dispersed therein. Thus, the mechanism for controlling the release of the active agent relies on the properties of the continuous hydrophilic phase, with the *discontinuous* silicone phase, in some embodiments, having pressure sensitive adhesive properties to secure the composition to the skin of a patient. Thus, the two compositions, and their respective mechanisms for controlling the release of active agent, are quite different.

Kosal does not address, nor does he solve, any problem relating to the controlled release of an active agent from an adhesive composition. Bott, on the other hand, is directed to a water-in-oil composition and relies upon a very different mechanism for the controlled release of an active agent. One must ask, what would Kosal fairly suggest to one skilled in the art? Applicants submit that, at best, the skilled person might be motivated to use the Kosal silicone pressure sensitive adhesive compositions as the oil/hydrophobic phase of the water-in-oil topical preparation of Bott. However, such a combination would not result in the claimed oil-in-water emulsion wherein the active agent is in the continuous (hydrophilic) phase.

Moreover, Kosal's teaching at col. 5 that his adhesive can be used in personal care and medical applications still contains no suggestion of an oil-in-water emulsion in which the hydrophilic phase comprises a protein active agent. Even if Bott were to be consulted, Bott, to the contrary, would direct the skilled person to use a water-in-oil emulsion. This, in fact, teaches away from the present claimed subject matter. Applicants submit that the Examiner has failed to establish, by evidence or reasoning, a prima facie case for obviousness of the claimed subject matter. And, at best, even if such teachings were to be combined, the claimed subject matter would not result.

As for dependent claims 74-86, applicants submit that as they depend directly or indirectly from patentable independent claim 72, those claims are patentable for the same reasons that claim 72 is patentable as discussed in detail above. Further, as claim 90 recites a method of using the composition of claim 72, claim 90 is patentable for the same reasons that claim 72 is patentable.

With respect to claims 87-88 which are directed to a multi-layer dressing, the Examiner has cited to Woodard et al. (US 4655767) for its teaching of a transdermal drug delivery device having multiple layers. The Examiner does not explicitly state a motivation for combining the reference teachings other than to allude to the rejection of claim 72 over Kosal and Bott and the fact that Woodard evidences "the state of the art" (Action, p. 6). Nor does the Examiner propose any specific modifications or substitutions in any of the compositions of Kosal or Bott or the construction of Woodard. Moreover, in Woodard's construction, either the pressure sensitive adhesive layer does not contact the drug-impregnated elastomer 20 at all (see space 24 in Fig. 2) or is positioned so as to separate the drug-impregnated elastomer 20 from a patient's skin (col. 3, lines 25-30). Applicants' multi-layer dressing positions the controlled release composition so that it will be directly against the skin of a patient, with the pressure sensitive adhesive located between the controlled release composition and one or more of a backing layer, cushioning layer, absorbent layer, and second adhesive layer (see, e.g., Figs. 1A-1D). Accordingly, even if the reference teachings were to be combined in the manner proposed by the Examiner (which manner has certainly not been made clear in the Action), the construction would be different than the subject matter of claims 87-88.

Applicants reiterate, as discussed in detail above, that Kosal contains no suggestion of an oil-in-water emulsion in which the hydrophilic phase comprises a protein active agent. Even if

Bott were to be consulted, Bott, to the contrary, would direct the skilled person to use a water-in-oil emulsion. Applicants submit that the Examiner has failed to establish, by evidence or reasoning, a prima facie case for obviousness of the claimed subject matter. And, at best, even if such teachings were to be combined, the claimed subject matter would not result.

Finally, with respect to the rejection of claim 89, the Examiner concedes, as she must, that Kosal does not teach or suggest a controlled release layer free of water. Indeed, as discussed above, Kosal is silent concerning any controlled release of an active agent properties that his adhesive may or may not possess. And, while Bott teaches an embodiment using a dry patch, again, Bott teaches a water-in-oil emulsion, not an oil-in-water emulsion. The reference teachings are not combinable in the manner proposed by the Examiner. Even if those teachings were to be combined, the claimed subject matter would not result because Bott, which is the only reference that relates to the controlled release of an active agent, explicitly teaches one to use a water-in-oil emulsion.

Conclusion

Applicants submit that for all of the reasons discussed above, the rejections are not well taken and should be withdrawn. It is believed that the above represents a complete response to the rejections set forth in the Official Action, and places the present application in condition for allowance. Reconsideration and an early allowance are requested.

Respectfully submitted,
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